HEPATITIS C
August 2003

1: Acta Gastroenterol Belg. 2003 Jan-Mar;66(1):15-9.
Hepatitis C: screening, treatment and prevention practical guidelines.
Michielsen P, Brenard R, Bourgeois N, De Galocsy Ch, Delwaide J, Henrion J, Horsmans Y, Nevens F, Reynaert H, Robaeys G, Sprengers D, Van Vlierberghe H; Steering Committee Belgian Association for the Study of the Liver.
Department of Hepatogastroenterology, University Hospital Antwerp, Wilrijkstraat 10, 2650 Edegem. peter.michielsen@uza.be
PMID: 12812144 [PubMed - indexed for MEDLINE]

2: Adv Nurse Pract. 2003 Jun;11(6):63-6, 68, 70.
Liver disease and HIV. Hepatitis is an ongoing threat.
Johnson D, Cohen S, Bonacini M.
University of Southern California, Los Angeles, USA.
PMID: 12807059 [PubMed - indexed for MEDLINE]

3: AIDS Policy Law. 2003 Jun 20;18(12):7.
Hemophiliacs sue Bayer over contaminated blood products.
[No authors listed]
PMID: 12846189 [PubMed - indexed for MEDLINE]

4: AIDS Read. 2003 Jul;13(7):346-7.
Comment on:
AIDS Read. 2003 Jul;13(7):344-8.
Editorial comment: drug-drug interactions, hepatitis C, and mitochondrial toxicity.
Glesby MJ, Gerber JG.
PMID: 12889453 [PubMed - indexed for MEDLINE]

5: AIDS Read. 2003 Jul;13(7):344-8.
Comment in:
AIDS Read. 2003 Jul;13(7):346-7.
Fatal lactic acidosis and pancreatitis associated with ribavirin and didanosine therapy.
Butt AA.
University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA.
Pancreatitis and lactic acidosis are severe and life-threatening adverse events associated with nucleoside analogue antiretroviral therapy used to treat HIV infection. The drug from this class most commonly associated with these adverse events is stavudine, although zidovudine and didanosine have also been implicated. Ribavirin is a nucleoside analogue used in combination with interferon alfa to treat hepatitis C. Because of similar mechanisms of action, the combination of these 2 drugs could potentially increase such toxicity. A case of fatal lactic acidosis and pancreatitis is described in an HIV-infected patient coinfected wtih hepatitis C on a didanosine-containing antiretroviral regimen after treatment of hepatitis C was

initiated with ribavirin and pegylated interferon alfa-2b. Extreme caution should be exercised when
didanosine and ribavirin are used concomitantly because of the increased risk of mitochondrial toxicity and the syndrome of severe metabolic acidosis with elevated lactic acid levels.
PMID: 12889452 [PubMed - indexed for MEDLINE]

6: AIDS Read. 2003 Jun;13(6):288-90.
Comment on:
AIDS Read. 2003 Jun;13(6):279-80, 287.
Editorial comment: diagnosis of acute HIV infection in hepatitis C treatment nonresponders--is extra vigilance required?
Golia P, Talal A.
PMID: 12846174 [PubMed - indexed for MEDLINE]

7: AIDS Read. 2003 Jun;13(6):279-80, 287.
Comment in:
AIDS Read. 2003 Jun;13(6):288-90.
Acute HIV seroconversion in a patient receiving pegylated interferon for treatment of hepatitis C.
Maser E, Dieterich DT.
University of Toronto, Toronto, Canada.
Hepatitis C is diagnosed frequently in persons with HIV infection. However, the diagnosis of HIV infection during treatment of hepatitis C has not been reported. We present a case of acute HIV seroconversion in a patient who was not responding to interferon therapy for treatment of hepatitis C.
PMID: 12846173 [PubMed - indexed for MEDLINE]

8: AIDS Treat News. 2000 May 5;(342):5.
Prison and HIV or hepatitis: June 17 meeting in Washington.
[No authors listed]
An important one-day meeting on several issues affecting prisoners with HIV and/or hepatitis is being sponsored by the ACLU.
PMID: 12870460 [PubMed - indexed for MEDLINE]

9: Am J Gastroenterol. 2003 Jun;98(6):1384-90.
Changes in antipyrine clearance and platelet count, but not conventional liver tests, correlate with fibrotic change in chronic hepatitis C: value for predicting fibrotic progression.
Coverdale SA, Samarasinghe DA, Lin R, Kench J, Byth K, Khan MH, Crewe E, Liddle C, George J, Farrell GC.
The Storr Liver Unit, Westmead Millennium Institute, University of Sydney, Westmead Hospital, NSW, Australia.
OBJECTIVE: We tested whether fibrotic progression in chronic hepatitis C could be predicted by liver tests, antipyrine clearance, or platelet count. METHODS: In 58 patients (6 untreated, 52 interferon-treated), a second liver biopsy was taken median 4.5 yr after first histologic diagnosis. We used receiver operating characteristic curves to determine whether changes in conventional liver tests, antipyrine clearance, or platelet count were predictive of altered hepatic fibrosis score. RESULTS: Apart from a weak association with change in ALT, conventional liver tests (albumin, bilirubin, prothrombin time) failed to correlate with changes (Delta) in hepatic fibrosis, but there were significant correlations between deltaantipyrine clearance or deltaplatelet count and deltafibrosis score ($p < 0.01$). As indicated by areas under the receiver operating characteristic curves, the diagnostic accuracy of deltaantipyrine clearance for fibrotic progression was 68%; for

Deltaplatelet count it was 80%. With defined cut-off values (-0.05 ml/min/kg for deltaantipyrine clearance; -41 x 10(9)/L for deltaplatelet count), the negative predictive values for fibrotic progression were 85% with antipyrine clearance and 89% with platelet count. Corresponding positive predictive values were 48% and 91%, respectively.
CONCLUSIONS: Changes in antipyrine clearance and platelet count are more sensitive than conventional tests for indicating fibrotic change in chronic hepatitis C. Both could be used to reliably identify those who do not have fibrotic progression, and platelet count also has a high positive predictive value for disease progression.
PMID: 12818285 [PubMed - indexed for MEDLINE]

10: Am J Gastroenterol. 2003 Jun;98(6):1377-83.
Sequence analysis of PePHD within HCV E2 region and correlation with resistance of interferon therapy in Japanese patients infected with HCV genotypes 2a and 2b.
Saito T, Ito T, Ishiko H, Yonaha M, Morikawa K, Miyokawa A, Mitamura K.
Seond Department of Internal Medicine, Showa University School of Medicine, Tokyo, Japan.
OBJECTIVE: Hepatitis C virus (HCV) E2 protein was recently reported to have a double-stranded RNA-activated protein kinase-eukaryotic initiation factor 2alpha (PKR-eIF2alpha) phosphorylation homology domain (PePHD); PKR is induced by interferon (IFN). PePHD interacts with PKR and inactivates it. PePHD could be a predictor for IFN response, like the interferon sensitivity determination region (ISDR) of HCV NS5A. Several groups reported that PePHD is conserved, and mutations in this region do not correlate with IFN response. In this study, we further investigated the amino acid variation of PePHD among four major genotypes and its correlation with IFN response. METHODS: We enrolled 74 patients for this study and determined PePHD sequence of HCV derived from sera of patients infected with HCV genotype 1a (1 patient; nonresponder [NR]), 1b (36 patients; 4 complete responders [CR], 32 NR), 2a (29 patients; 17 CR, 12 NR), and 2b (8 patients; 3 CR, 5 NR). We also analyzed mutations in ISDR of HCV genotype 1b in 31 patients. RESULTS: PePHD had several variations among four
genotypes investigated. In patients infected with HCV genotype 1b, PePHD sequence was well conserved and seemed to have no correlation with IFN response. Mutations in ISDR were correlated with IFN response. In patients with HCV genotypes 2a and 2b, PePHD had multiple variations, and one particular motif, "RGQQ-" at the N-terminus, showed a close correlation with IFN resistance. All eight patients with HCV containing this motif were IFN nonresponders.
CONCLUSIONS: IFN resistance of HCV correlates with its "RGQQ-" motif at the N-terminus of PePHD in HCV genotype 2a and 2b. PePHD of HCV could be a predictor of IFN resistance in patients infected with HCV genotype 2a and 2b.
PMID: 12818284 [PubMed - indexed for MEDLINE]

11: Am J Gastroenterol. 2003 May;98(5):952-5.
Comment on:
Am J Gastroenterol. 2003 May;98(5):1135-41.
A link between leptin and steatosis in chronic hepatitis C? Time to weigh up the fats.
Patel K, Muir A, McHutchison JG, Patton HM.
PMID: 12809813 [PubMed - indexed for MEDLINE]

12: Am J Gastroenterol. 2003 May;98(5):1159-66.
Comparison of three commercially available assays for HCV RNA using the international unit standard: implications for management of patients with chronic hepatitis C virus infection in clinical practice.
Shiffman ML, Ferreira-Gonzalez A, Reddy KR, Sterling RK, Luketic VA, Stravitz RT, Sanyal AJ, Garrett CT, De Medina M, Schiff ER.

Hepatology Section, Virginia Commonwealth University Health System-Medical College of Virginia, Richmond, Virginia 23298, USA.
OBJECTIVES: The present study was performed to evaluate the impact of the international unit standard for measuring HCV RNA in the management of patients with chronic hepatitis C virus (HCV) infection. METHODS: The three assays used were Amplicor Monitor PCR, the National Genetics Institute PCR assay, and branched chain DNA. HCV RNA was measured at four time points (baseline, 3 months after the start of therapy, at the end of treatment, and 6 months after discontinuation of therapy) in 106 consecutive patients who received interferon and ribavirin for chronic HCV. RESULTS: The mean age of the patients was 44 yr. Of the patients, 62% were male, 24% were African American, 38% had bridging fibrosis or cirrhosis, and 75% were HCV genotype 1. Of the 424 samples analyzed, 82-89% of values were within 1 log unit and 85-92% were within 2 log units by the various assays. This variability was not dependent upon HCV genotype. HCV RNA was undetectable in 1.4-6.8% of samples when virus was detected by another assay. The mean HCV RNA in these discordant samples was 1.47-6.33 log IU/ml (30-2,100,000 IU/ml). CONCLUSIONS: These data demonstrate that approximately 90% of serum values for HCV RNA were within 1 log unit by the international unit standard regardless of which virological assay was used. However, false positive and false negative results as well as variations in the HCV RNA level of more than 1 to 2 log units can occur with any of the assays, and these results may have an impact upon the management of patients receiving interferon therapy. It is therefore unwise in clinical practice to base important treatment decisions upon a single HCV RNA determination.
PMID: 12809843 [PubMed - indexed for MEDLINE]

13: Am J Gastroenterol. 2003 May;98(5):1135-41.
Comment in:
Am J Gastroenterol. 2003 May;98(5):952-5.
Serum leptin levels correlate with hepatic steatosis in chronic hepatitis C.
Romero-Gomez M, Castellano-Megias VM, Grande L, Irles JA, Cruz M, Nogales MC, Alcon JC, Robles A.
Units of Hepatology, Hospital Universitario de Valme, Sevilla, Spain.
OBJECTIVES: Hepatic steatosis (HS) has been related to obesity and fibrosis in chronic hepatitis C (CHC). The aim of this study was to determine the role of leptin system in HS development. METHODS: Patients (n = 131) with biopsy-proven CHC, positive HCV RNA, and raised ALT were enrolled. Body mass index, percentage of body fat by skin fold measurement, and bioelectrical impedance analysis was calculated and serum leptin concentration measured. Intrahepatic HCV RNA, HS, necroinflammatory activity, and fibrosis were determined in liver biopsy tissue. RESULTS: HS was present in 63 patients (48.1%). Steatosis was evident in 32 of 91 patients (35.2%) infected with genotype 1 and in 22 of 27 patients (81.5%) with genotype 3a ($p < 0.001$). In patients infected by genotype 3a, HS correlated significantly with intrahepatic HCV RNA load ($r = 0.78$; $p < 0.001$). However, in genotype 1, HS was associated with host factors such as leptin, body mass index, percentage of body fat, and visceral obesity. Multivariate analysis showed genotype (OR = 11.54, 95% CI = 1.13-117.14, p = 0.038), leptin levels (OR = 1.09, 95% CI = 1.03-1.17, p = 0.008) and fibrosis (OR = 9.86, 95% CI = 2.11-5.86, p = 0.03) as independent variables of HS development. CONCLUSIONS: Hepatic steatosis was related to genotype, fibrosis degree, and serum leptin levels. Genotype 3 seems to have a viral specific steatogenic effect. Leptin seems to be a link between obesity and steatosis development in CHC genotype 1-infected patients.
PMID: 12809839 [PubMed - indexed for MEDLINE]

14: Am J Gastroenterol. 2003 May;98(5):1142-9.

Hepatic metallothionein in patients with chronic hepatitis C: relationship with severity of liver disease and response to treatment.
Carrera G, Paternain JL, Carrere N, Folch J, Courtade-Saidi M, Orfila C, Vinel JP, Alric L, Pipy B.
Laboratory of Macrophage, Inflammatory Mediators and Cellular Interactions, Institut Louis Bugnard, Centre Hospitalier Universitaire Rangueil, Toulouse Cedex, France.
OBJECTIVES: Reactive oxygen species may be involved in the pathogenesis of chronic hepatitis C virus infection. Metallothionein (MT) is an essential protein for the protection of cells against reactive oxygen species. The aim ofthis prospective study was to assess the influence of the hepatic level andcellular distribution of MT in hepatitis C virus (HCV) infection and in the
liver disease outcome. METHODS: In liver biopsy samples of 32 patients with chronic HCV infection and of 12 control subjects, quantification of MT was performed by radioimmunoassay, MT, interleukin (IL)-1 and -6, and tumor necrosis factor (INF)-alpha mRNA by reverse transcription-polymerase chain reaction (PCR) and cellular distribution by immunohistochemistry. RESULTS: In HCV-infected patients, MT liver protein level was 3-fold lower than in control specimens. A significant inverse linear regression between MT protein or mRNA expression and the Histological Activity Index, the necroinflammatory grade, and the stage of fibrosis was observed. MT immunostaining was located in the nucleus and cytoplasm in hepatocytes of control subjects, whereas it was mainly cytoplasmic in HCV-infected patients. Before interferon (IFN) therapy, the hepatic MT level in patients that were nonsustained responders was half that of sustained responders. Intrahepatic IL-6 and MT were simultaneously down-regulated, but no correlation was found between MT and intrahepatic cytokine mRNA expression in patients with chronic HCV infection. CONCLUSIONS: This study shows that hepatic MT expression could reflect the severity of chronic HCV infection and could be one of the factors associated with a favorable clinical outcome in the response to interferon therapy.
PMID: 12809840 [PubMed - indexed for MEDLINE]

15: Am J Gastroenterol. 2003 May;98(5):1150-4.
Hepatitis C virus-associated hypobetalipoproteinemia is correlated with plasma viral load, steatosis, and liver fibrosis. Petit JM, Benichou M, Duvillard L, Jooste V, Bour JB, Minello A, Verges B, Brun JM, Gambert P, Hillon P. Services de Diabetologie et Endocrinologie, Dijon cedex, France.
OBJECTIVES: A relationship between chronic hepatitis C virus (HCV) infection and lipid metabolism has recently been suggested. The aim of this study was to determine the correlation between lipid profile and virology, histologic lesions, and response to alpha interferon therapy in noncirrhotic, nondiabetic patients with hepatitis C. METHODS: A total of 109 consecutive untreated chronic hepatitis C patients were studied to assess the following: 1) the effects of HCV genotype, viral load, steatosis, hepatic fibrosis, and body mass index (BMI) on
lipid profile; and 2) whether lipid parameters could predict response to antiviral therapy. RESULTS: The control group showed a significantly higher apolipoprotein B (apoB) concentration compared with patients with chronic hepatitis C. Hypobetalipoproteinemia (apo B <0.7 g/L) was found in 27 (24.7%) chronic HCV patients and in five (5.3%) control subjects ($p = 0.0002$). Levels of apo B were negatively correlated with steatosis and HCV viral load ($r = -0.22$; $p = 0.03$). This last correlation was strong for non-1 genotype and genotype 3 ($r = -0.48$; $p = 0.0005$, and $r = -0.47$; $p = 0.007$, respectively) but was not found in genotype 1. In multivariate analysis, low apo B concentration was significantly associated with fibrosis grade 2 or 3 versus grade 0 or 1 ($p < 0.001$), steatosis >5% ($p < 0.001$), low body mass index ($p < 0.001$), and high HCV viral load ($p < 0.014$). No correlation was found in the 76 treated patients between apo B and response to

interferon therapy. CONCLUSIONS: In chronic HCV patients, hypobetalipoproteinemia occurs already in the early stages of HCV infection before the development of liver cirrhosis. The correlation between apo B levels and HCV viral load seems to confirm the interaction between hepatitis C infection and beta-lipoprotein metabolism.
PMID: 12809841 [PubMed - indexed for MEDLINE]

16: Am J Infect Control. 2003 Jun;31(4):215-20.
Investigation of infection control practices and knowledge of hepatitis C among body-piercing practitioners. Hellard M, Aitken C, Mackintosh A, Ridge A, Bowden S. Epidemiology and Social Research Unit, Macfarlane Burnet Institute for Medical Research and Public Health, PO Box 254, Fairfield, Victoria, Australia 3078.
BACKGROUND: Body piercing has become increasingly popular, leading to concerns about the associated risk of hepatitis C virus (HCV) transmission during piercing. Many body-piercing practitioners (BPPs) have recently entered the industry but little is known about their training and understanding of HCV transmission. This study measured BPP knowledge about HCV and infection control procedures. It also tested for HCV contamination within body-piercing establishments. METHODS: BPPs completed a questionnaire about the number and type of piercings performed, their methods for disposing of and reprocessing piercing equipment, and their training and knowledge of HCV. Environmental swabs were collected and tested for HCV RNA. RESULTS: BPPs at 35 establishments were recruited. A total of 31 BPPs had training as a BPP, ranging from 1 hour to 6 years (median: 15 days). Reprocessing of equipment was variable; 8 establishments inadequately reprocessed piercing guns and 4 inadequately reprocessed forceps or guiding equipment. All BPPs were aware of HCV but many did not know how the virus was transmitted. A total of 19 BPPs performed extra cleaning after piercing a customer known to be HCV positive. No environmental swabs tested were positive for HCV RNA. CONCLUSIONS: This study showed that many BPPs had inadequate training, and lacked knowledge and understanding of HCV transmission, infection control, and universal precautions. To reduce the risk of HCV transmission, BPPs should be required to undergo formal training in
infection control before being registered as BPPs.
PMID: 12806358 [PubMed - indexed for MEDLINE]

17: Am J Med. 2003 Jun 15;114(9):765-7.
Cases from the Osler Medical Service at Johns Hopkins University.
Dharmadhikari A, Sukkar A, Mani S.
PMID: 12829205 [PubMed - indexed for MEDLINE]

18: Am J Trop Med Hyg. 2003 Apr;68(4):501-2.
Infection with human herpesvirus-8 and its correlation with hepatitis B virus and hepatitis C virus markers among rural populations in Cambodia.
Sarmati L, Andreoni M, Suligoi B, Bugarini R, Uccella I, Pozio E, Rezza G.
Department of Public Health, Tor Vergata University, Rome, Italy.
sarmati@med.uniroma2.it
Among 164 individuals in a rural population of Cambodia, antibodies to human herpesvirus-8 (HHV-8) were found among 56.6% of the women and 50.6% of the men. Seropositivity for HHV-8 tended to decrease with age ($P < 0.001$) and was not associated with exposure to hepatitis B virus (HBV) or HCV. Human herpesvirus-8, which shows a high rate of infection during childhood, does not seem to have the same pattern of transmission as HBV. This suggests very early acquisition of infection with HHV-8 in Cambodia.
PMID: 12875304 [PubMed - indexed for MEDLINE]

19: Ann Intern Med. 2003 Jul 1;139(1):46-50.
Test characteristics of alpha-fetoprotein for detecting hepatocellular carcinoma in patients with hepatitis C. A systematic review and critical analysis.
Gupta S, Bent S, Kohlwes J.
University of California, San Francisco, USA.
BACKGROUND: Patients with hepatitis C virus (HCV) are at increased risk for hepatocellular carcinoma. Although serum alpha-fetoprotein (AFP) is often used to detect hepatocellular carcinoma in HCV-infected individuals, its utility is unclear. PURPOSE: To define the test characteristics of AFP for the diagnosis of hepatocellular carcinoma in patients with HCV. DATA SOURCES: MEDLINE search from 1966 to December 2002 for English- and non-English-language articles examining the test characteristics of AFP for identifying hepatocellular carcinoma. STUDY SELECTION: Articles were included if they reported the sensitivity and specificity of AFP for detecting hepatocellular carcinoma in patients with HCV. Articles were excluded if the cause of hepatitis was ambiguous or if 50% or more of the study patients did not have HCV. DATA EXTRACTION: Relevant articles were evaluated for quality of evidence; test characteristics were abstracted and calculated. DATA SYNTHESIS: Five studies met all inclusion criteria and were analyzed. The overall quality of evidence was limited; only one study universally applied an acceptable gold standard test, and three of five studies used a case-control design that potentially overestimates diagnostic accuracy. By using the most commonly reported cutoff value of a positive test result for hepatocellular carcinoma (AFP level > 20 microg/L), the ranges of test characteristics were as follows: sensitivity, 41% to 65%; specificity, 80% to 94%; positive likelihood ratios, 3.1 to 6.8; and negative likelihood ratios, 0.4 to 0.6. CONCLUSIONS: The paucity of high-quality data calls for more rigorous study of AFP and other diagnostic tests for detecting hepatocellular carcinoma in HCV-infected patients with an accepted gold standard applied to the entire cohort. Even if the "best-case" estimates of AFP sensitivity and specificity are accurate, AFP has limited utility for detecting hepatocellular carcinoma.
PMID: 12834318 [PubMed - indexed for MEDLINE]

20: Ann Trop Med Parasitol. 2003 Mar;97(2):187-92.
Infection with hepatitis B and C viruses and human retroviruses (HTLV-I and HIV) among high-risk Lebanese patients.
Ramia S, Klayme S, Naman R.
Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon. sramia@aub.edu.lb
Three groups of Lebanese patients (haemophiliacs, patients on cycled cancer chemotherapy who were regularly receiving blood transfusions, and intravenous drug users) and a control group of healthy blood donors were checked for markers of infection with hepatitis viruses (B and C) and human retroviruses (HIV and HTLV-I). Compared with the controls, all three groups of patients were more likely to be seropositive for antibody to hepatitis C virus (anti-HCV), and the haemophiliacs and cancer patients (but not the relatively young drug users) were more likely to be seropositive for hepatitis B virus (HBV). All the haemophiliacs and cancer patients found to be carrying the surface antigen of HBV (HBsAg) and/or to be seropositive for anti-HCV had given the same result when tested before the screening of blood and blood products for HBsAg and anti-HCV became routine practice in Lebanon (a decade before the present study). The four intravenous drug users (IVDU) found seropositive for HBV (two cases) or anti-HCV (two cases) had seroconverted in the 2 years prior to the present study. In addition to highlighting the problem of HCV infection among IVDU, the present results emphasise the need for the careful screening of donated blood for all blood-borne viruses, and for the exclusive use of

disposable equipment in the management of cancer patients. The anti-HBV vaccination of IVDU is
recommended but only the results of further clinical evaluation will show whether the similar vaccination of patients on cycled cancer chemotherapy is of value. Although none of the patients or controls was found positive for anti-HIV-1, anti-HIV-2 or anti-HTLV-I, the routine screening of blood and blood products for these viruses (particularly for HIV) should remain mandatory.
PMID: 12803874 [PubMed - indexed for MEDLINE]

21: AORN J. 2003 Jun;77(6):1191-6, 1200-4; quiz 1206, 1211-2.
The silent dragon--hepatitis C.
Walker B, Howard L.
Franciscan Health System, Tacoma, Wash, USA.
The hepatitis C virus is the most common bloodborne pathogen in the world. A disease with no cure or vaccine, it kills between 8,000 and 10,000 people annually in the United States. Only recently have experts begun to understand the virus, its natural progression, and how it differs from other hepatitis viruses. Most transmission is a result of direct percutaneous exposure, and the disease is more common among minority groups. Alpha interferon and ribavirin are the currently approved first-line treatment medications. Evolving medication therapies, full liver transplantation from nonliving donors, and split liver transplantation from living donors hold promise for the 170 million people who are thought to carry the virus.
PMID: 12817742 [PubMed - indexed for MEDLINE]

22: Arch Intern Med. 2003 Jun 23;163(12):1489-90; author reply 1490.
Comment on:
Arch Intern Med. 2002 Oct 14;162(18):2141-2.
Management of health care workers with blood-borne infections.
Magnavita N, Placentino RA, Puro V, Sacco A.
PMID: 12824103 [PubMed - indexed for MEDLINE]

23: Care Manag J. 2002 Summer;3(4):160-5.
Hepatitis C: what every case manager should know.
Beckerman NL, Grube-Farrell B.
Yeshiva University, Wurzweiler School of Social Work, 2495 Amsterdam Ave., New York, NY 10033, USA. beckerma@ymail.yu.edu
Over the next decade, case managers can anticipate encountering increasing numbers of clients with hepatitis C. This article provides a sociopolitical and medical overview of hepatitis C, diagnosis, risk and transmission factors, co-infection of HIV and hepatitis C treatment issues. The article identifies and analyzes policy and practice implications for case managers in health care.
PMID: 12847931 [PubMed - indexed for MEDLINE]

24: Chest. 2003 Jul;124(1):406-10.
Pegylated interferon and ribavirin-induced interstitial pneumonitis with ARDS.
Abi-Nassif S, Mark EJ, Fogel RB, Hallisey RK Jr.
Department of Pharmacy, Division of Pulmonary and Critical Care, and Massachusetts General Hospital, Boston, MA 02114, USA. sabinassif@partners.org
A 49-year-old man with cirrhosis due to hepatitis C virus developed interstitial pneumonitis documented by surgical lung biopsy specimen evaluation after two weekly doses of pegylated interferon-alpha(2)b in combination with ribavirin. He developed ARDS and died after 26 days of hospitalization from multisystem organ failure. This case suggests that interstitial pulmonary disease can occur with pegylated interferon-alpha(2)b therapy.
PMID: 12853555 [PubMed - indexed for MEDLINE]

25: Clin Immunol. 2003 Jul;108(1):46-50.
The Delta 32 mutation of the chemokine-receptor 5 gene neither is correlated with chronic hepatitis C nor does it predict response to therapy with interferon-alpha and ribavirin.
Glas J, Torok HP, Simperl C, Konig A, Martin K, Schmidt F, Schaefer M, Schiemann U, Folwaczny C.
Medizinische Klinik, Klinikum der Ludwig-Maximilians Universitat Munchen, Standort Innenstadt, Munich, Germany.
Unlike in HIV, homozygosity for a 32-bp deletion (Delta 32) of the chemokine receptor 5 (CCR5) gene was recently described in increased frequency in patients with chronic hepatitis C (HCV). Thus, it was speculated that this mutation might be relevant for disease susceptibility and influence the response to antiviral therapy. The present study sought to confirm the association between HCV and the Delta 32 mutation of the CCR5 gene and to correlate it with the response to therapy with interferon-alpha-2a and ribavirin. Sixty-two patients with HCV and 119 healthy unrelated controls were genotyped for the Delta 32 mutation. For the correlation between the Delta 32 mutation and response to therapy, only patients (n = 59) who completed 6 months of combination therapy as part of a prospective study were evaluated. The Delta 32 mutation was not observed in increased frequency in HCV. Furthermore, a significant difference of the HCV load or aminotransferase concentrations was not observed in carriers versus noncarriers of the Delta 32 mutation. After stratification for potentially confounding factors such as gender or HCV genotype, a significant difference was also not detected with respect to treatment outcome. These observations argue strongly against a role of CCR5 for susceptibility to HCV infection or response to combination therapy.
PMID: 12865070 [PubMed - indexed for MEDLINE]

26: Clin Infect Dis. 2003 Jul 15;37(2):314; author reply 314-5.
Comment on:
Clin Infect Dis. 2002 Oct 15;35(8):966-73.
Detection of hepatitis C virus RNA in normal cervical smears.
Wang C, Polyak SJ, Corey L.
PMID: 12856226 [PubMed - indexed for MEDLINE]

27: Clin Infect Dis. 2003 Jul 1;37(1):33-40. Epub 2003 Jun 24.
Factors associated with hepatitis C virus infection in injection and noninjection drug users in Italy.
Quaglio G, Lugoboni F, Pajusco B, Sarti M, Talamini G, Lechi A, Mezzelani P, Des Jarlais DC.
Medical Service for Addictive Disorders and Department of Internal Medicine, University of Verona, 37134 Verona, Italy. paolo.mezzelani@univr.it
We describe the prevalence of hepatitis C virus (HCV) infection among noninjection users of heroin in Italy and compare the prevalence of HCV infection among noninjection drug users (NIDUs) and injection drug users (IDUs). Multiple logistic regression analysis of data from NIDUs showed that hepatitis B virus (HBV) infection status was the only independent predictor of HCV seroprevalence. Among IDUs, the number of years of drug use and HBV and human immunodeficiency virus infection status were independent predictors of HCV seropositivity. We found an HCV infection prevalence of 20% among NIDUs. This rate was much lower than that for IDUs, who are 11 times more likely to have antibodies against HCV. The prevalence of HCV infection was much higher than that of HBV infection among the IDUs. In contrast, the prevalence of HBV infection was slightly higher than that of HCV infection among unvaccinated

NIDUs. The prevalence of HCV infection among long-term IDUs approached true population saturation; among long-term NIDUs, however, it appeared to plateau at approximately 40%. Additional research on HCV infection among NIDUs is needed to develop a strategic prevention program for this patient subgroup.
PMID: 12830406 [PubMed - indexed for MEDLINE]

28: Clin Infect Dis. 2003 Jun 15;36(12):1564-71. Epub 2003 Jun 03.
Comparison of 2 regimens that include interferon-alpha-2a plus ribavirin for treatment of chronic hepatitis C in human immunodeficiency virus-coinfected patients.
Neau D, Trimoulet P, Winnock M, Rullier A, Le Bail B, Lacoste D, Ragnaud JM, Bioulac-Sage P, Lafon ME, Chene G, Dupon M; ROCO Study Group.
Federation des Maladies Infectieuses, Centre Hospitalo-Universitaire Pellegrin, Bordeaux, France. didier.neau@chu-bordeaux.fr
An open-label, randomized trial was conducted to compare the efficacy and safety of 2 regimens of interferon-alpha-2a (IFN-alpha-2a) plus ribavirin for management of chronic hepatitis C virus (HCV) infection in human immunodeficiency virus (HIV)-coinfected patients. Sixty-eight patients were randomized to receive IFN-alpha-2a at a dosage of either (1) 6 MU given 3 times per week for 24 weeks, followed by 3 MU 3 times per week for an additional 24
weeks (group A; 31 patients); or (2) 9 MU per day for 2 weeks, followed by 3 MU per day for 22 weeks, followed by 3 MU 3 times per week for 24 weeks (group B; 37 patients). Ribavirin was added at week 16 of therapy if HCV RNA remained detectable at week 12. Sustained virological response was achieved in 10 patients (15%; 6 in group A and 4 in group B). HCV genotypes 2 or 3 and a decrease in the HCV load of >or=3 log(10) copies/mL between inclusion and week 4
were associated with virological response. In conclusion, the combination of conventional IFN-alpha-2a and ribavirin has poor virological efficacy in HCV-HIV-coinfected patients.
PMID: 12802757 [PubMed - indexed for MEDLINE]

29: Clin Infect Dis. 2003 Jun 15;36(12):1632-4.
Very rapid evolution of infection with hepatitis C virus transmitted by an accidental needlestick.
Garcia JM, Serrano PL, Terron Sdel C, Marugan RB, Garcia GM, Grande LG, Miquel J, Plaza AG.
PMID: 12802777 [PubMed - indexed for MEDLINE]

30: Cochrane Database Syst Rev. 2003;(2):CD003181.
Bile acids for viral hepatitis.
Chen W, Liu J, Gluud C.
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BACKGROUND: The viral hepatitides are common causes of liver diseases globally. Trials have assessed bile acids for patients with viral hepatitis, but no consensus was reached regarding their usefulness. OBJECTIVES: To assess the beneficial and harmful effects of bile acids for viral hepatitis. SEARCH STRATEGY: Searches were performed of the trial registers of The Cochrane Hepato-Biliary Group (September 2002), The Cochrane Library (Issue 2, 2002),
MEDLINE (September 2002), EMBASE (September 2002), and The Chinese Biomedical
Database (April 2001). SELECTION CRITERIA: Randomised clinical trials comparing any dose or duration of bile acids versus placebo or no intervention for viral hepatitis were included, irrespective of language, publication status, or blinding. DATA COLLECTION AND ANALYSIS: Two reviewers extracted the data independently. The

methodological quality of the trials was evaluated with respect to generation of the allocation sequence, allocation concealment, double blinding, and follow-up. The outcomes were presented as relative risks (RR) or weighted mean differences (WMD) with 95% confidence intervals (CI). MAIN
RESULTS: We identified 27 randomised trials of bile acids for hepatitis B or C; none were of high methodological quality. In one trial, ursodeoxycholic acid (UDCA) versus placebo for acute hepatitis B significantly reduced the risk of hepatitis B surface antigen positivity at the end of treatment and serum HBV DNA level at the end of follow-up. In another trial, UDCA versus no intervention for chronic hepatitis B significantly reduced the risk of having abnormal serum
transaminase activities at the end of treatment. Twenty-five trials compared bile acids (21 trials UDCA; four trials tauro-UDCA) versus placebo or no intervention with or without conterventions for chronic hepatitis C. Bile acids did not significantly reduce the risk of having detectable serum HCV RNA (RR 0.99, 95% CI 0.91 to 1.07), cirrhosis, or portal and periportal inflammation
score at the end of treatment. Bile acids significantly decreased the risk of having abnormal serum alanine aminotransferase activity at the end of treatment (RR 0.82, 95% CI 0.76 to 0.90) and follow-up (RR 0.91, 95% CI 0.85 to 0.98). Bile acids significantly increased the Knodell score (WMD 0.20, 95% CI 0.08 to 0.31) at the end of treatment. No severe adverse events were reported. We did not identify trials including patients with hepatitis A, acute C, D, or E.
REVIEWER'S CONCLUSIONS: Bile acids lead to a significant improvement in serum transaminase activities in hepatitis B and C. There is insufficient evidence either to support or to refute effects on viral markers, mortality, incidence of cirrhosis, or liver histology. Trials with high methodological quality are required.
PMID: 12804455 [PubMed - indexed for MEDLINE]

31: Dig Dis Sci. 2003 Jun;48(6):1124-9.
Interferon-alpha2b induction treatment with or without ribavirin in chronic hepatitis C: a multicenter, randomized, controlled trial.
Senturk H, Ersoz G, Ozaras R, Kaymakoglu S, Bozkaya H, Akdogan M, Mert A, Bozdayi M, Tabak F, Yenice N, Ozbay G.
Department of Internal Medicine, Cerrahpasa Medical Faculty, Istanbul University, Istanbul, Turkey.
We aimed to compare the efficacy of interferon-alpha2b (IFN) induction treatment in combination with ribavirin to IFN induction alone in chronic hepatitis C. In total, 125 patients (66 male, 59 female, mean age: 48 +/- 9, range: 21-70) were enrolled and randomized into two arms: In the first, patients received 5 MU/day of IFN for 4 weeks followed by 3 MU/day for the next 4 weeks. Treatment was continued with 3 MU three times a week IFN for an additional 40 weeks. Ribavirin was administered 1000-1200 mg/day according to the body weight for the entire 48-week period. In the second arm, patients received placebo in addition to IFN.
Fifty-nine patients were placed in the ribavirin arm and 66 in placebo arm. All patients were genotype 1. At week 48, 24/66 (36%) from the placebo and 31/59 (52%) from the ribavirin group responded (P > 0.05). However, during the 24-week untreated follow-up period, 13/24 (54%) from the placebo, and 8/31 (26%) from the ribavirin group relapsed (P = 0.002.), resulting in a sustained virologic response (SVR) rate of 17% in the placebo and 39% in the ribavirin group (P = 0.005.) In conclusion, IFN induction treatment in combination with ribavirin is superior to IFN induction treatment alone in genotype 1 patients, and the SVR rate of 39% is encouraging.
PMID: 12822874 [PubMed - indexed for MEDLINE]

32: Epidemiol Infect. 2003 Jun;130(3):501-5.
Genotypes of hepatitis C virus circulating in Tunisia.

Djebbi A, Triki H, Bahri O, Cheikh I, Sadraoui A, Ben Ammar A, Dellagi K.
Laboratory of Clinical Virology, Institut Pasteur, Tunis, Tunisia.
Hepatitis C virus (HCV) isolates from 93 patients living in Tunisia, including 16 haemophiliacs, were genotyped by INNO LiPA and partial sequencing of the 5' untranslated region of the viral genome. In non-haemophiliacs, subtype 1b was largely predominant (79%), types 1a, 2a, 2b, 3a and 4a occurred much less frequently at 5, 7, 3, 3 and 1% of cases, respectively. In the group of haemophiliacs, a co-dominance between subtypes 1a and 1b was noticed (38%). Type
distribution of HCV in Tunisia differs from that reported in other countries of the Mediterranean and Middle East regions. Genotyping results in respect of clinical status, age, and genotyping methods, are discussed.
PMID: 12825736 [PubMed - indexed for MEDLINE]

33: Epidemiol Infect. 2003 Jun;130(3):497-500.
Prevalence and risk factors of HIV, hepatitis B and hepatitis C in a forensic population of rapists and child molesters.
Giotakos O, Bourtsoukli P, Paraskeyopoulou T, Spandoni P, Stasinos S, Boulougouri D, Spirakou E.
Psychiatry Department and Research & Prevention Unit, Tripolis' General Army Hospital, 22100 Tripolis, Greece.
The aim of the present study was to assess the prevalence as well as the possible risk factors of HIV, hepatitis B and hepatitis C, in 194 male prisonerswho had been convicted for rape (n = 105) or child molestation (n = 89). HBsAg, HBeAg, anti-HBc, anti-HBs, anti-HCV and anti-HIV-1/2 were tested for. The participants also completed a standard sociodemographic questionnaire, indicating possible risk factors, the Barratt Impulsiveness Scale, and the
life-time history of aggression. Anti-HIV antibodies were not found in any of the prisoners. HBsAg was found in 25 (13%), anti-HBc in 94 (49%), anti-HBs in 40 (21%) and anti-HCV in 13 (6.5%) subjects. Logistic regression analysis showed that anti-HCV positivity was associated with intravenous drug use (OR 20.7, 95% CI 1.1-4.9, P<0.001), while HBsAg positivity was associated separately with being foreign (OR 4.0, 95% CI 0.2-2.5, P<0.1), as well as with impulsiveness score (OR 1.06, 95% CI 0.01-0.11, P<0.02). The prevalence of HBV and HCV
infection in this sex offender sample was highly increased in relation to the general population. Since it has been proved that sex offenders are a high-risk group for reoffending, monitoring their health is a necessary step towards prevention of sexually transmitted diseases being spread.
PMID: 12825735 [PubMed - indexed for MEDLINE]

34: Fam Community Health. 2002 Oct;25(3):61-70.
A community-based free nursing clinic's approach to management of health problems for the uninsured: the hepatitis C example.
Van Zandt SE, D'Lugoff MI, Kelley L.
Johns Hopkins University School of Nursing, Baltimore, Maryland, USA.
Poverty, as an outgrowth of lack of opportunity in employment, basic education, affordable housing, and racism, directly affects disparities in health status. Health care providers are challenged to identify and overcome systemic barriers to health services for the poorest patients. This article describes the population of patients and the model of care offered by the Wald Community Nursing Center, a free nurse-managed clinic in Baltimore, Maryland. Hepatitis C infection is used to illustrate the confounding factors of a costly, chronic health problem and the interventions that have been instituted to overcome them.
PMID: 12802143 [PubMed - indexed for MEDLINE]

35: Gastroenterology. 2003 Jul;125(1):80-8.
Comment in:
Gastroenterology. 2003 Jul;125(1):253-6.
Acute hepatitis C: high rate of both spontaneous and treatment-induced viral clearance.
Gerlach JT, Diepolder HM, Zachoval R, Gruener NH, Jung MC, Ulsenheimer A, Schraut WW, Schirren CA, Waechtler M, Backmund M, Pape GR.
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BACKGROUND & AIMS: Acute hepatitis C virus infection accounts for approximately 20% of cases of acute hepatitis today. The aim of this study was to define the natural course of the disease and to contribute to the development of treatment strategies for acute hepatitis C virus. METHODS: The diagnosis of acute hepatitis C virus in 60 patients was based on seroconversion to anti-hepatitis C virus antibodies or clinical and biochemical criteria and on the presence of hepatitis C virus RNA in the first serum sample. RESULTS: Fifty-one of 60 (85%)
patients presented with symptomatic acute hepatitis C virus. In the natural (untreated) course of acute symptomatic hepatitis C (n = 46), spontaneous clearance was observed in 24 patients (52%), usually within 12 weeks after the onset of symptoms, whereas all asymptomatic patients (n = 9) developed chronic hepatitis C. The start of antiviral therapy (interferon-alpha with or without ribavirin) beyond 3 months after the onset of acute hepatitis induced sustained
viral clearance in 80% of treated patients. CONCLUSIONS: The management of acute
hepatitis C has to take into account the high rate of spontaneous viral clearance within 12 weeks after the onset of symptomatic disease. Treatment of only those patients who remain hepatitis C virus RNA positive for more than 3 months after the onset of disease led to an overall viral clearance (self-limited and treatment induced) in 91% of patients, and unnecessary
treatment was avoided in those with spontaneous viral clearance. Patients with asymptomatic acute hepatitis C virus infection are unlikely to clear the infection spontaneously and should be treated as early as possible.
PMID: 12851873 [PubMed - indexed for MEDLINE]

36: Gastroenterology. 2003 Jul;125(1):253-6.
Comment on:
Gastroenterology. 2003 Jul;125(1):80-8.
New insights into acute hepatitis C.
Gordon SC.
PMID: 12851890 [PubMed - indexed for MEDLINE]

37: Gastroenterology. 2003 Jun;124(7):2003-4; author reply 2004-5.
Comment on:
Gastroenterology. 2002 May;122(5):1303-13.
Weight-based ribavirin with pegylated interferon alfa 2b: benefits, risks, and the origin of the evidence.
Hrachovec J, Patel P.
PMID: 12812198 [PubMed - indexed for MEDLINE]

38: Gastroenterology. 2003 Jun;124(7):1946-9.
Spontaneous resolution of chronic hepatitis C virus disease after withdrawal of immunosuppression.
Somsouk M, Lauer GM, Casson D, Terella A, Day CL, Walker BD, Chung RT.

Gastrointestinal Unit, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, 32 Fruit Street, Boston, MA 02114, USA.
Approximately 85% of acute cases of hepatitis C infection result in chronic hepatitis. Spontaneous clearance of hepatitis C virus has been thought to occur exclusively after acute infection and is associated with a robust cellular immune response. We describe here a case of a renal transplant recipient who acquired posttransplant hepatitis C virus infection with rapid histological progression but who subsequently experienced spontaneous viral clearance along
with histological remission after removal of immunosuppression. Immunologic studies showed persistently strong cellular immune responses. This case underscores the importance of restoration of the immune system in the control of hepatitis C virus viremia and disease progression and the need to minimize or obviate immunosuppression in organ transplant recipients.
PMID: 12806627 [PubMed - indexed for MEDLINE]

39: Hepatology. 2003 Jul;38(1):4-13.

Kinetics of the immune response during HBV and HCV infection.

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The innate immune system has a role not only in protecting the host during the initial period of virus infection, but also in shaping the nature of the adaptive immune response. In this review, we follow the kinetics of the virologic and immunologic events occurring from the time of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection. We primarily discuss how the early
events after infection might influence the development of the adaptive immune response in these 2 important viral infections and how new strategies for more efficient preventive and therapeutic vaccines can be derived from this knowledge.
PMID: 12829979 [PubMed - indexed for MEDLINE]

40: Hepatology. 2003 Jul;38(1):21-4.
Comment on:
Hepatology. 2003 Jul;38(1):66-74.
Ribavirin as maintenance therapy for hepatitis C patients: an interim peacekeeper?
Patel K, Dev A, Muir AJ, McHutchison JG.
PMID: 12829982 [PubMed - indexed for MEDLINE]

41: Hepatology. 2003 Jul;38(1):25-33.

Liver transplantation with hepatitis C virus-infected graft: interaction between donor and recipient viral strains.
Fan X, Lang DM, Xu Y, Lyra AC, Yusim K, Everhart JE, Korber BT, Perelson AS, Di Bisceglie AM.
Division of Gastroenterology and Hepatology, Saint Louis University, St. Louis, MO, USA.
Superinfection of different viral strains within a single host provides an opportunity for studying host-virus and virus-virus interactions, including viral interference and genetic recombination, which cannot be studied in infections with single viral strains. Hepatitis C virus (HCV) is a positive single-strand RNA virus that establishes persistent infection in as many as 85%
of infected individuals. However, there are few reports regarding coinfection or superinfection of HCV. Because of the lack of tissue culture systems and small animal

models supporting efficient HCV replication, we explored these issues in the setting of liver transplantation where both recipient and donor were infected with different HCV strains and therefore represent a distinct model for HCV superinfection. Serial serum samples collected at multiple time points were obtained from 6 HCV-positive liver donor/recipient pairs from the National Institute of Diabetes and Digestive and Kidney Diseases liver transplantation database. At each time point, HCV genotype was determined by both restriction fragment length polymorphism analysis and phylogenetic analysis. Furthermore, we selectively sequenced 3 full-length HCV isolates at the earliest time points after liver transplantation, including both 5' and 3' ends. Detailed genetic
analyses showed that only one strain of HCV could be identified at each time point in all 6 cases. Recipient HCV strains took over in 3 cases, whereas donor HCV strains dominated after liver transplantation in the remaining 3 cases. In conclusion, in all 6 cases studied, there was no genetic recombination detected among HCV quasispecies or between donor and recipient HCV strains.
PMID: 12829983 [PubMed - indexed for MEDLINE]

42: Hepatology. 2003 Jul;38(1):34-41.
A model to predict severe HCV-related disease following liver transplantation.
Berenguer M, Crippin J, Gish R, Bass N, Bostrom A, Netto G, Alonzo J, Garcia-Kennedy R, Rayon JM, Wright TL.

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Post-transplantation recurrence is increasing in patients with HCV. Early antiviral therapy may be of benefit in this setting. Thus, accurate and early prediction of progression may help select candidates for treatment. We developed a model based on pre- and/or early post-transplantation variables, which may predict progression to severe disease. Clinical and histologic outcomes were assessed in 554 liver recipients. A total of 1,353 biopsy specimens obtained after 1 year (median of 2 biopsies per patient; range, 1-8) were scored. Two
outcome measures were used: cumulative probability of developing severe disease (fibrosis 3 and 4) within 5 years and actual progression to severe disease in 2 years. We used Cox proportional hazard survival analysis for the whole cohort. Predictors analyzed included HCV genotype and recipient, donor, and transplant-related variables. The cumulative risk of progressing to fibrosis 3 and 4 was significantly greater in patients transplanted recently ($P < .001$) and was present in all centers. Factors increasing this risk were genotype, induction with mycophenolate, donor age, short course of azathioprine, and prednisone (<12 months). To create a model of prediction, 285 patients with 2-year follow-up were used to create a logistic regression analysis. The estimated probability of being at high risk for severe disease was calculated from a formula that included donor age and recipient therapy as critical variables. In conclusion, we have developed a model that uses early post-transplantation variables to predict severe HCV recurrence. Accuracy of the model is not perfect (c-statistic 0.80), probably reflecting the complexity of HCV in the liver transplant setting.
PMID: 12829984 [PubMed - indexed for MEDLINE]

43: Hepatology. 2003 Jul;38(1):42-9.
Moderate alcohol consumption increases oxidative stress in patients with chronic hepatitis C.
Rigamonti C, Mottaran E, Reale E, Rolla R, Cipriani V, Capelli F, Boldorini R, Vidali M, Sartori M, Albano E.
Internal Medicine Unit, Ospedale Maggiore della Carita, Novara, Italy.

The mechanisms by which alcohol consumption worsens the evolution of chronic hepatitis C (CHC) are poorly understood. We have investigated the possible interaction between hepatitis C virus (HCV) and ethanol in promoting oxidative stress. Circulating IgG against human serum albumin (HSA) adducted with malondialdehyde (MDA-HSA), 4-hydroxynonenal (HNE-HSA), or arachidonic acid hydroperoxide (AAHP-HSA) and against oxidized cardiolipin (Ox-CL) were evaluated as markers of oxidative stress in 145 CHC patients with different alcohol consumption, 20 HCV-free heavy drinkers (HD) without liver disease, and 50 healthy controls. Anti-MDA IgG was increased in CHC patients irrespective of alcohol intake as well as in the HD group. CHC patients with moderate alcohol intake (<50 g ethanol/d), but not HD, also had significantly higher values of anti-AAHP-HSA, anti-HNE-HSA, and anti-Ox-CL IgG (P <.05) than controls. A further elevation (P <.001) of these antibodies was evident in CHC patients with
heavy alcohol intake (>50 g ethanol/d). Anti-AAHP and anti-Ox-CL IgG above the 95th percentile in the controls were observed in 24% to 26% of moderate and 58% to 63% of heavy drinkers but only in 6% to 9% of the abstainers. The risk of developing oxidative stress during CHC was increased 3-fold by moderate and 13-to 24-fold by heavy alcohol consumption. Heavy drinking CHC patients had significantly more piecemeal necrosis and fibrosis than abstainers. Diffuse piecemeal necrosis was 4-fold more frequent among alcohol-consuming patients
with lipid peroxidation-related antibodies than among those without these antibodies. In conclusion, even moderate alcohol consumption promotes oxidative stress in CHC patients, suggesting a role for oxidative injury in the worsening of CHC evolution by alcohol.
PMID: 12829985 [PubMed - indexed for MEDLINE]

44: Hepatology. 2003 Jul;38(1):50-6.

Hepatitis C virus infection and incident type 2 diabetes.

Mehta SH, Brancati FL, Strathdee SA, Pankow JS, Netski D, Coresh J, Szklo M, Thomas DL.

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Although hepatitis C virus (HCV) infection is more common among adults with type 2 diabetes, it is uncertain whether HCV precedes the development of diabetes. Thus, we performed a prospective (case-cohort) analysis to examine if persons who acquired type 2 diabetes were more likely to have had antecedent HCV infection when enrolled in a community-based cohort of men and women between the ages of 44 and 65 in the United States (Atherosclerosis Risk in Communities Study [ARIC]). Among 1,084 adults free of diabetes at baseline, 548 developed
diabetes over 9 years of follow-up evaluation. Incident cases of diabetes were identified by using fasting glucose and medical history and HCV antibodies were assessed at baseline. A priori, persons were categorized as low-risk or high-risk for diabetes based on their age and body mass index, factors that appeared to modify the type 2 diabetes-HCV infection incidence estimates. The overall prevalence of HCV in this population was 0.8%. Among those at high risk
for diabetes, persons with HCV infection were more than 11 times as likely as those without HCV infection to develop diabetes (relative hazard, 11.58; 95% confidence interval, 1.39-96.6). Among those at low risk, no increased incidence of diabetes was detected among HCV-infected persons (relative hazard, 0.48; 95% confidence

interval, 0.05-4.40). In conclusion, pre-existing HCV infection may increase the risk for type 2 diabetes in persons with recognized diabetes risk
factors. Additional larger prospective evaluations are needed to confirm these preliminary findings.
PMID: 12829986 [PubMed - indexed for MEDLINE]

45: Hepatology. 2003 Jul;38(1):57-65.
Alcohol potentiates hepatitis C virus replicon expression.
Zhang T, Li Y, Lai JP, Douglas SD, Metzger DS, O'Brien CP, Ho WZ.
Division of Allergy and Immunology, Joseph Stokes Jr. Research Institute at The Children's Hospital of Philadelphia, Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA 19104, USA.
Alcohol consumption accelerates liver damage and diminishes the anti-hepatitis C virus (HCV) effect of interferon alfa (IFN-alpha) in patients with HCV infection. It is unknown, however, whether alcohol enhances HCV replication and promotes HCV disease progression. The availability of the HCV replicon containing hepatic cells has provided a unique opportunity to investigate the interaction between alcohol and HCV replicon expression. We determined whether alcohol enhances HCV RNA expression in the replicon containing hepatic cells.
Alcohol, in a concentration-dependent fashion, significantly increased HCV replicon expression. Alcohol also compromised the anti-HCV effect of IFN-alpha. Investigation of the mechanism(s) responsible for the alcohol action on HCV replicon indicated that alcohol activated nuclear factor kappaB (NF-kappaB) promoter. Caffeic acid phenethyl ester (CAPE), a specific inhibitor of the
activation of NF-kappaB, abolished alcohol-induced HCV RNA expression. In addition, naltrexone, an opiate receptor antagonist, abrogated the enhancing effect of alcohol on HCV replicon expression. In conclusion, alcohol, probably through the activation of NF-kappaB and the endogenous opioid system, enhances HCV replicon expression and compromises the anti-HCV effect of IFN-alpha. Thus, alcohol may play an important role in vivo as a cofactor in HCV disease progression and compromise IFN-alpha-based therapy against HCV infection.
PMID: 12829987 [PubMed - indexed for MEDLINE]

46: Hepatology. 2003 Jul;38(1):66-74.
Comment in:
Hepatology. 2003 Jul;38(1):21-4.
Maintenance therapy with ribavirin in patients with chronic hepatitis C who fail to respond to combination therapy with interferon alfa and ribavirin.
Hoofnagle JH, Ghany MG, Kleiner DE, Doo E, Heller T, Promrat K, Ong J, Khokhar F, Soza A, Herion D, Park Y, Everhart JE, Liang TJ.
Liver Diseases Section, Digestive Diseases Branch, and Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892, USA.
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To assess the efficacy and safety of maintenance therapy with ribavirin alone in chronic hepatitis C, 108 patients were treated with the combination of interferon alfa and ribavirin for 24 weeks; those who failed to have a virologic response were offered enrollment in a randomized, double-blind, controlled trial of ribavirin (1,000-1,200 mg daily) versus placebo for the subsequent 48 weeks. Patients were monitored at regular intervals with symptom questionnaires, serum aminotransferase levels, hepatitis C virus (HCV) RNA levels, and complete blood counts and underwent liver biopsy at the completion of therapy. Among 108 patients, 50 were still HCV RNA positive after 24 weeks of treatment, of whom 34 agreed to be randomized to continue either ribavirin monotherapy or placebo. Among 17 patients who received placebo, there was no overall improvement in

symptoms, serum alanine aminotransferase (ALT) levels, HCV RNA levels, or hepatic histology. Among the 17 patients who received ribavirin, serum ALT levels and necroinflammatory features of liver histology were improved, whereas symptoms, HCV RNA levels, and hepatic fibrosis scores were not changed significantly from baseline. Responses to ribavirin seemed to be categorical, such that 8 patients (47%) had definite improvement in liver histology. Patients with improved histology had improvements in serum ALT levels both on combination therapy and after switching to ribavirin monotherapy. In conclusion, continuation of ribavirin monotherapy may maintain serum biochemical improvements that occur during interferon-ribavirin combination therapy in some patients and that these improvements are often associated with decreases in necroinflammatory changes in the liver. Whether these improvements will ultimately result in prevention of progression of hepatitis C requires further study.
PMID: 12829988 [PubMed - indexed for MEDLINE]

47: Hepatology. 2003 Jul;38(1):75-85.
Effect of treatment with peginterferon or interferon alfa-2b and ribavirin on steatosis in patients infected with hepatitis C.
Poynard T, Ratziu V, McHutchison J, Manns M, Goodman Z, Zeuzem S, Younossi Z, Albrecht J.
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It has been suggested that hepatitis C virus (HCV) and especially genotype 3 is associated with steatosis. We assess the effect of treatment with peginterferon or interferon alfa-2b and ribavirin on steatosis. We analyzed 1,428 naïve patients included in a randomized trial. A single pathologist scored steatosis at baseline and 24 weeks after the treatment. At baseline, steatosis was present in 935 of 1,428 patients (65%), including 175 (83%) of 210 patients with genotype 3 versus 760 (62%) of 1,218 with other genotypes (P <.001). The variables associated with steatosis in logistic regression were genotype 3 (P <.001), triglycerides greater than 1.7 mmol/L (P <.001), body mass index greater than 27 (P <.04), age greater than 40 years (P <.001), and septal fibrosis (P =.007). In genotype 3-infected patients, steatosis was associated with high viral load and with lower serum cholesterol. Steatosis was associated with lower sustained response rate, even after taking into account other factors (P <.001). Among virologic responders, steatosis was much improved in genotype 3, improvement of at least 1 grade in 77%, and disappearance in 46% compared with other genotypes, 46% and 29%, respectively (P <.001 both comparisons). In genotype 3 responders, the baseline low serum cholesterol was corrected by treatment (P <.001). Steatosis was associated with HCV genotype 3, triglycerides, high body mass index, age, fibrosis stage, and lower virologic response to treatment. In conclusion, sustained disappearance of the virus is associated with reduction of steatosis in genotype 3 as well as a correction of baseline low serum cholesterol.
PMID: 12829989 [PubMed - indexed for MEDLINE]

48: Hepatology. 2003 Jul;38(1):270-1.
Serotype 3 is most common hepatitis C serotype in Pakistan: however, significant numbers are untypeable.
Khokhar N, Asif N, Khokhar OS.
PMID: 12830013 [PubMed - indexed for MEDLINE]

49: Hepatology. 2003 Jul;38(1):269; author reply 270.
Comment on:

Hepatology. 2003 Mar;37(3):520-7.
Screening for hepatocellular carcinoma in high-risk patients: Western versus Eastern virus.
Huo TI, Lee SD, Wu JC.
PMID: 12830012 [PubMed - indexed for MEDLINE]

50: Hepatology. 2003 Jul;38(1):267-8; author reply 268-9.
Comment on:
Hepatology. 2003 Jan;37(1):65-71.
Interleukin 1beta gene polymorphism and hepatitis C virus-related hepatocellular carcinoma.
Yeo AE, Tanaka Y, Furuta T.
PMID: 12830011 [PubMed - indexed for MEDLINE]

51: Hepatology. 2003 Jul;38(1):267.
Comment on:
Hepatology. 2002 Nov;36(5):1273-9.
Mortality rate during interferon alfa-ribavirin combination therapy of chronic hepatitis C.
Soza A, Hoofnagle JH.
PMID: 12830010 [PubMed - indexed for MEDLINE]

52: Hum Pathol. 2003 Jun;34(6):573-9.
The dermatopathologic manifestations of hepatitis C infection: a clinical, histological, and molecular assessment of 35 cases.
Crowson AN, Nuovo G, Ferri C, Magro CM.
Centeral Medical Laboratories, Winnipeg, Manitoba, Canada.
Cutaneous eruptions related to hepatitis C virus (HCV), a major cause of hepatitis in the setting of blood transfusion, intravenous drug abuse, organ transplantation, and hemodialysis, are typically reported as isolated cases. We encountered 35 cases of HCV infection associated with cutaneous eruptions. The present study evaluates paraffin-embedded, formalin-fixed tissue sections stained with hematoxylin and eosin from biopsy specimens of skin lesions from 35
patients seropositive for HCV. In 20 cases, reverse transcriptase polymerase chain reaction (RT-PCR) was performed using a probe for HCV RNA; the RNA was detected through the action of alkaline phosphatase on the chromogen nitroblue tetrazolium and bromochloroindolyl phosphate. The clinical spectrum comprised dermatomyositis-like photodistributed eruptions, palpable purpura, folliculitis, violaceous and perniotic acral lesions, ulcers, nodules, and urticaria. Lesions were also classified histopathologically by the dominant reaction pattern:
vasculopathies of neutrophilic, lymphocytic, and granulomatous vasculitis and pauci-inflammatory subtypes (15 patients); palisading granulomatous inflammation (3 patients); sterile neutrophilic folliculitis (5 patients); dermatitis herpetiformis (1 patient); lobular panniculitis composed of neutrophilic lobular panniculitis in 2 patients and benign cutaneous polyarteritis nodosa in 1 patient; neutrophilic dermatoses, including neutrophilic urticaria, neutrophilic
eccrine hidradenitis, and pyoderma gangrenosum (3 patients); interface dermatitis (3 patients); and low-grade lymphoproliferative disease of B-cell lineage representing marginal zone lymphoma in 1 patient and a clonal plasmacellular infiltrate in another patient. In most cases, whereas 1 of the aforementioned disorders defined the dominant reaction pattern, there was an
accompanying secondary reaction pattern, defining a hybrid picture. Endothelial changes including endothelial cell enlargement and effaced heterochromatin with

margination of the chromatin to the nuclear membrane were seen in several cases; in some cases similar cytopathic changes also involved the supporting pericytes, eccrine ductular cells, or keratinocytes. The RT-PCR analyses in 8 of 20 cases examined revealed HCV RNA expression in a focal, weak fashion in endothelia and perivascular inflammatory cells in those cases showing vasculopathic changes. Viral parasitism of endothelia may be important in cutaneous lesional propagation in the setting of HCV infection. Cross-reactivity between endogenous
and viral antigens, leading to cellular and/or type II immune reactions; viral tropism to B lymphocytes, resulting in B cell expansion with resultant autoantibody production; and circulating immune complexes containing monoclonal cryoglobulins may also be of pathogenetic importance. Tropism of the virus to B lymphocytes provides a mechanism for the development of low-grade clonal B cell lymphoproliferative disease in this setting.
PMID: 12827611 [PubMed - indexed for MEDLINE]

53: Infection. 2003 Jun;31(3):194-6.
Hepatitis C virus infection and cancer risk among HIV-infected individuals.
Pradier C, Carrieri MP, Piche M, Rosenthal E, Dellamonica P, Serraino D.
PMID: 12836634 [PubMed - indexed for MEDLINE]

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Hepatitis C: past, present, future. Abstracts of an international conference. Dublin, Ireland, 25-27 June 2003.
[No authors listed]
PMID: 12868439 [PubMed - indexed for MEDLINE]

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Correlation of single photon emission computed tomography parameters as a noninvasive alternative to liver biopsies in assessing liver involvement in the setting of HIV and hepatitis C virus coinfection: a multicenter trial of the Adult AIDS Clinical Trials Group.
Shiramizu B, Theodore D, Bassett R, Coel M, Sherman KE, Glesby MJ, Chow D, Alston B, Colquhoun D, Merigan TC Jr, Reichman RC, Berggren R, Burning WJ, Brobst S; Adult AIDS Clinical Trials Group 5096 Team.
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Performing a liver biopsy in patients infected with HIV and hepatitis C virus (HCV) is considered the standard of practice to assess hepatic involvement but carries risks to patients. This pilot study was designed to identify single photon emission computed tomography (SPECT) parameters that correlate with liver disease stage. HIV-coinfected and HCV-coinfected individuals undergoing a liver biopsy had a SPECT scan performed. The results showed that a number of SPECT parameters were associated with histologic changes in architecture, fibrosis,
and cirrhosis, of which two SPECT parameters, the minimum pixel count for spleen region of interest and maximum pixel count for right hepatic lobe, correctly classified 39 of 46 SPECT/biopsy pairs. In conclusion, this pilot trial identified SPECT parameters that correlated with liver histology changes. A larger study is needed to demonstrate whether SPECT parameters alone or with other markers can provide information on fibrosis with the clinical significance obtained through liver biopsy.
PMID: 12843743 [PubMed - indexed for MEDLINE]

56: J Acquir Immune Defic Syndr. 2003 Jul 1;33(3):365-72.
The impact of hepatitis C virus coinfection on HIV progression before and after highly active antiretroviral therapy.
Klein MB, Lalonde RG, Suissa S.

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To compare the impact of hepatitis C virus (HCV) coinfection on progression of HIV infection in the eras before and after the introduction of highly active antiretroviral therapy (HAART), the authors conducted a retrospective cohort study. One hundred twenty-five HCV+ patients and 1076 HCV- patients were studied; 83% of HCV+ patients were injection drug users. HCV+ subjects experienced no clear benefit from HAART. The adjusted hazard ratios (HRs) of
opportunistic infection, death, and hospitalization were 0.74 (95% CI: 0.31-1.78), 1.78 (95% CI: 0.59-5.37), and 2.1 (95% CI: 0.90-4.90), respectively, comparing the post-HAART era with the pre-HAART era. In contrast, HCV- subjects experienced rate reductions for all outcomes. Comparable HRs for opportunistic infection, death, and hospitalization were 0.49 (95% CI: 0.37-0.64), 0.28 (95% CI: 0.19-0.41), and 0.51 (95% CI: 0.38-0.67), respectively. HCV+ subjects
remained at increased risk for death and hospitalization post-HAART even after additional adjustment for antiretroviral use and time-updated CD4 cell and viral load measures. Deaths and hospitalizations in HCV+ patients were primarily for non-AIDS-defining infections and complications of injection drug use. HCV coinfection and comorbidity associated with injection drug use are preventing the realization of substantial health benefits associated with HAART.
PMID: 12843748 [PubMed - indexed for MEDLINE]

57: J Acquir Immune Defic Syndr. 2003 Jul 1;33(3):356-64.
The association of hepatitis C prevalence, activity, and genotype with HIV infection in a cohort of New York City drug users.
Strasfeld L, Lo Y, Netski D, Thomas DL, Klein RS.
Division of Infectious Diseases, Department of Medicine, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, New York 10467, USA.
Factors associated with serum HCV antibody, HCV RNA level, and HCV genotype were
assessed in 557 current and former drug users. Additional assays included HIV antibody, CD4+ lymphocyte counts, HIV viral loads, and hepatitis B markers. Seventy-five percent of subjects were anti-HCV positive, of whom 75% had detectable HCV RNA (median, 5.04 x 10(5) IU/mL; range, 1020-15.7 x 10(6)). On multivariate analysis HCV seropositivity was associated with history of drug injection, HIV seropositivity, and increased age and inversely with drug
snorting. Among anti-HCV-positive persons, detectable HCV RNA was independently associated with HIV seropositivity, male gender, and history of injection and inversely associated with hepatitis B surface antigen positivity. Among persons with detectable HCV RNA, higher levels were independently associated with higher HIV viral load, increased age, and genotypes 2a and 2b. These findings demonstrate an association of HCV RNA level with HIV viral load, independent of the level of immunosuppression. However, a substantial degree of the person-to-person variability in the prevalence and level of detectable HCV RNA
remains unexplained.
PMID: 12843747 [PubMed - indexed for MEDLINE]

58: J Acquir Immune Defic Syndr. 2003 Jul 1;33(3):373-9.
HIV and hepatitis C virus risk in new and longer-term injecting drug users in Oslo, Norway.
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Research has focused on understanding injecting drug use initiation in the era of HIV/AIDS. However, differences between new and longer-term injecting drug users (IDUs) have not received as much attention. This study examined injecting initiation experience, risk and risk reduction practices, and self-reported HIV and hepatitis C virus (HCV) testing practices and infection among new (injecting < or =4 years) and longer-term IDUs. Data from 3 cross-sectional surveys in 1992, 1994, and 1997 of syringe exchange program (SEP) users in Oslo, Norway,
were used. Approximately one fifth of IDUs were new injectors. New IDUs were increasingly indistinguishable from longer-term IDUs in terms of socio-demographics, risk practices, and HIV and HCV testing. The prevalence of HIV infection remained low (5%); in contrast, approximately two thirds of all SEP users reported being HCV-infected. Known HCV infection status had no impact on syringe sharing; most HCV-infected SEP users reported sharing syringes, regardless of the duration of injecting. The only variable associated with HCV infection was injecting < or =4 years (adjusted odds ratio = 0.2; 95% confidence interval = 0.1-0.4). Increased similarity in age between new and longer-term IDUs may have contributed to the rapid spread of HCV infection by facilitating mixing patterns between HCV-infected and -susceptible IDUs.
PMID: 12843749 [PubMed - indexed for MEDLINE]

59: J Clin Psychiatry. 2003 Jun;64(6):708-14.
Psychiatric symptoms in patients with chronic hepatitis C receiving interferon alfa-2b therapy.
Kraus MR, Schafer A, Faller H, Csef H, Scheurlen M.
Clinic for Internal Medicine, University of Wurzburg, Germany. m.kraus@mail.uni-wuerzburg.de
BACKGROUND: Psychiatric side effects of interferon alfa are frequently observed in the therapy of patients with chronic hepatitis C infection. The goal of the present study was to assess prospectively the incidence, spectrum, and extent of psychiatric symptoms of patients receiving interferon alfa therapy as compared with an untreated reference group. METHOD: 104 patients with chronic hepatitis C were consecutively enrolled in a prospective longitudinal study. The treatment group (N = 84) received interferon alfa-2b for up to 12 months, and the reference group (N = 20) received no treatment. Patients who began treatment between November 1996 and August 1998 (N = 44) received interferon alfa-2b, 5 million units 3 times per week. Patients who began treatment in September 1998 or later (N = 40) received a combination of interferon alfa-2b, 3 to 5 million units 3 times per week, and ribavirin, 1000-1200 mg/day. Diagnostic scores for depression and anxiety were obtained by means of the psychometric instrument
Hospital Anxiety and Depression Scale, and scores for anger/hostility were obtained with the Symptom Checklist-90 Revised. RESULTS: In contrast to the untreated reference group, we found significantly increased scores for depression ($p < .001$) and anger/hostility ($p < .001$) during interferon alfa therapy in the treatment group. Even before therapy, scores of those in the
treatment group were above the respective cutoff values for clinically relevant symptoms of depression in 15.5% of the patients, anxiety in 13.1% of the patients, and anger/hostility in 11.3% of the patients. These proportions rose to 35.0% (depression), 25.6% (anxiety), and 24.5% (anger/hostility). The cumulative frequency of clinically relevant emotional distress (depression, anxiety, or anger/hostility) during interferon alfa therapy was 57.7%, as compared with 22.5% before therapy. However, interferon alfa therapy had to be stopped prematurely because of untreatable psychiatric symptoms in only 8.3% of patients.
CONCLUSION: In view of the high frequency and extent of psychiatric symptoms with interferon alfa therapy, we recommend a close follow-up of patients receiving this therapy with respect to potential limiting mood changes.

PMID: 12823087 [PubMed - indexed for MEDLINE]

60: J Drugs Dermatol. 2003 Jan;2(1):63-7.
Local blistering reaction complicating subcutaneous injection of pegylated interferon in a patient with hepatitis C.
Gallina K, Brodell RT, Naffah F, Nedorost S.
Northeastern Ohio Universities College of Medicine, Rootstown, Ohio, USA.
PEG-Intron is a covalent conjugate of recombinant alpha-2b interferon with monomethoxy polyethylene glycol (PEG). Compared to standard interferon-alpha injections, this preparation has a longer half-life allowing for once-weekly injections and superior antiviral efficacy in the treatment of hepatitis C when used in combination with ribavirin. We report the first case of a local blistering reaction developing in a patient receiving pegylated interferon-alpha-2b. Previous reports of local cutaneous reactions to standard and pegylated interferon-alpha are reviewed and the pathophysiological mechanisms are discussed.
PMID: 12852384 [PubMed - indexed for MEDLINE]

61: J Drugs Dermatol. 2002 Jul;1(1):72-5.
Mixed cryoglobulinemia secondary to interferon therapy for hepatitis C: case report & review of the literature.
Kimyai-Asadi A, Gohar K, Kang P, Usman A, Zenenberg R, Jih MH. Ronald O.
Perelman Department of Dermatology, New York University School of Medicine, 401 East 34th Street, S-6N, New York, NY 10016, USA. akimyai@yahoo.com
Mixed cryoglobulinemia is a systemic vasculitis associated with hepatitis C infection. We present a case of mixed cryoglobulinemia induced by interferon-alpha therapy for hepatitis C infection and review previous cases in which cryoglobulinemic symptom exacerbations were caused by interferon-alpha.
PMID: 12847761 [PubMed - indexed for MEDLINE]

62: J Endocrinol Invest. 2003 Mar;26(3):261-4.
Interferon-alpha-induced transient severe hypothyroidism in a patient with Graves' disease.
Braga-Basaria M, Basaria S.
*SEMPR, (Division of Endocrinology and Metabolism) Hospital de Clinicas da Universidade Federal do Parana, Curitiba, Brazil,
Interferons (IFNs) are proteins with anti-viral activity and are widely used in the treatment of patients with chronic hepatitis C virus (HCV) infection. The use of IFNs has resulted in thyroid dysfunction in a variety of ways. We report a case of a woman with hyperthyroidism due to Graves' disease who developed significant hypothyroidism during treatment with IFN-alpha 2a for HCV infection. However, after discontinuation of IFN-alpha 2a, hyperthyroidism recurred.
Potential mechanisms by which IFNs influence thyroid function are discussed.
PMID: 12809178 [PubMed - indexed for MEDLINE]

63: J Exp Med. 2003 Jun 16;197(12):1645-55.
Memory CD8+ T cells are required for protection from persistent hepatitis C virus infection.
Shoukry NH, Grakoui A, Houghton M, Chien DY, Ghrayeb J, Reimann KA, Walker CM.
Center for Vaccines and Immunity, Columbus Children's Research Institute, Columbus, OH 43205, USA.
Few hepatitis C virus (HCV) infections resolve spontaneously but those that do appear to afford protective immunity. Second infections are usually shorter in duration and are less likely to persist but mechanisms of virus control in immune individuals have not been identified. In this study we investigated whether memory

helper and/or cytotoxic T lymphocytes provide protection in chimpanzees serially reinfected with the virus. Clearance of the first infection
took 3-4 mo and coincided with the delayed onset of CD4+ and CD8+ T cell responses. High frequencies of memory T cells targeting multiple HCV proteins were stable over 7 yr of follow-up. Animals were infected for a second time to assess the protective role of memory T cells. In contrast to the prolonged course of the first infection, viremia was terminated within 14 d. Control of this second infection was kinetically linked to rapid acquisition of virus-specific cytolytic activity by liver resident CD8+ T cells and expansion of memory CD4+ and CD8+ T cells in blood. The importance of memory CD8+ T cells in control of HCV infection was confirmed by antibody-mediated depletion of this lymphocyte subset before a third infection. Virus replication was prolonged despite the presence of memory CD4+ T helper cells primed by the two prior infections and was not terminated until HCV-specific CD8+ T cells recovered in
the liver. These experiments demonstrate an essential role for memory CD8+ T cells in long-term protection from chronic hepatitis C.
PMID: 12810686 [PubMed - indexed for MEDLINE]

64: J Lab Clin Med. 2003 Jun;141(6):372-7.
Zinc treatment prevents lipid peroxidation and increases glutathione availability in Wilson's disease.
Farinati F, Cardin R, D'inca R, Naccarato R, Sturniolo GC.
Department of Surgical and Gastroenterological Sciences, University of Padua, Padua, Italy.
Oxidative and reductive mechanisms are important in Wilson's disease. In this study, we sought to evaluate tissue levels of glutathione and cysteine, an important detoxification system, and of malondialdehyde, a marker of lipoperoxidation, in patients with Wilson's disease receiving penicillamine or zinc treatment, in comparison with patients with chronic liver disease of
different origin. Concentrations of cysteine, reduced/oxidized glutathione, malondialdehyde, zinc, and copper were determined (with the use of high-pressure liquid chromatography, fluorimetry and atomic-absorption spectrophotometry) in liver-biopsy specimens from 24 patients with Wilson's disease (18 treated with zinc, 6 with penicillamine), 34 patients with chronic viral hepatitis, and 10 patients with alcoholic liver disease. In patients with Wilson's disease, the concentration of reduced glutathione was lower than that in patients with viral
hepatitis and as high as that in subjects with alcoholic liver damage. The cysteine level was significantly lower than those in the control groups, and the percentage of oxidized glutathione/total glutathione was higher than that in viral or alcoholic disease. Malondialdehyde levels were low, but when zinc- and penicillamine-treated patients were considered separately, only the former had low malondialdehyde levels. Zinc-treated patients had higher concentrations of reduced glutathione and a lower percentage of oxidized glutathione. In summary, patients with Wilson's disease have relevant glutathione depression, with low levels of reduced glutathione and cysteine and high concentrations of oxidized glutathione: This is prevented by zinc administration, which inhibits lipid peroxidation and increases glutathione availability.
PMID: 12819634 [PubMed - indexed for MEDLINE]

65: J Nephrol. 2003 May-Jun;16(3):417-20.
Sustained response with negative serum HCV-mRNA and disappearance of antibodies after interferon-alpha therapy in a kidney transplant recipient with chronic active viral hepatitis C.
Luciani G, Bossolo M, Muscaritol M, Panocchia N, Ferrante A, Nanni G, Piccioni E, Tazza L, Grillo RL, Fanelli FR, Castagneto M.

Institute of Clinical Surgery, Cattolica del S. Cuore University, Rome, Italy.
BACKGROUND: The use of interferon-alpha (IFN-alpha) to treat viral hepatitis C (HCV) occurring in kidney transplant recipients is controversial. This study reports an HCV patient successfully treated with IFN-alpha therapy achieving sustained response, negative serum HCV-mRNA and the disappearance of HCV antibodies, without impairment of renal function. METHOD: A young kidney transplant recipient developed a proven HCV infection 70 months
post-transplantation. The patient received IFN-alpha therapy, and for a 32-month follow-up period was evaluated clinically, serologically and virologically. RESULTS: IFN-alpha therapy resulted in normal transaminase activities within 2 months. Serum HCV-mRNA was negative after 4 weeks of treatment and is still negative. Ten months after IFN-alpha therapy withdrawal, the enzyme immunoassay revealed that HCV antibodies (HCVAb) were absent in the serum. IFN-alpha therapy was safe, well tolerated and renal function was not impaired.
PMID: 12832744 [PubMed - indexed for MEDLINE]

66: J Virol. 2003 Jul;77(14):7843-55.
Nonstructural protein precursor NS4A/B from hepatitis C virus alters function and ultrastructure of host secretory apparatus.
Konan KV, Giddings TH Jr, Ikeda M, Li K, Lemon SM, Kirkegaard K.
Department of Microbiology and Immunology, Stanford University School of Medicine, Stanford, CA, USA.
The nonstructural proteins of hepatitis C virus (HCV) have been shown previously to localize to the endoplasmic reticulum (ER) when expressed singly or in the context of other HCV proteins. To determine whether the expression of HCV nonstructural proteins alters ER function, we tested the effect of expression of NS2/3/4A, NS4A, NS4B, NS4A/B, NS4B/5A, NS5A, and NS5B from genotype 1b HCV on anterograde traffic from the ER to the Golgi apparatus. Only the nominal precursor protein NS4A/B affected the rate of ER-to-Golgi traffic, slowing the rate of Golgi-specific modification of the vesicular stomatitis virus G protein expressed by transfection by approximately threefold. This inhibition of ER-to-Golgi traffic was not observed upon expression of the processed proteins NS4A and NS4B, singly or in combination. To determine whether secretion of other cargo proteins was inhibited by NS4A/B expression, we monitored the appearance of newly synthesized proteins on the cell surface in the presence and absence of NS4A/B expression; levels of all were reduced in the presence of NS4A/B. This reduction is also seen in cells that contain genome length HCV replicons: the rate of appearance of major histocompatibility complex class I (MHC-I) on the cell surface was reduced by three- to fivefold compared to that for a cured cell line. The inhibition of protein secretion caused by NS4A/B does not correlate with the ultrastructural changes leading to the formation a "membranous web" (D. Egger et al., J. Virol. 76:5974-5984, 2002), which can be caused by expression
of NS4B alone. Inhibition of global ER-to-Golgi traffic could, by reducing cytokine secretion, MHC-I presentation, and transport of labile membrane proteins to the cell surface, have significant effects on the host immune response to HCV infection.
PMID: 12829824 [PubMed - indexed for MEDLINE]

67: J Virol. 2003 Jul;77(14):7914-23.
Frequent recovery and broad genotype 2 diversity characterize hepatitis C virus infection in Ghana, West Africa.

Candotti D, Temple J, Sarkodie F, Allain JP.
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Hepatitis C virus (HCV) infection is thought to mostly become chronic and rarely resolves. HCV infection was serologically screened in 4,984 samples from Ghanaian blood donors, and 1.3% prevalence was found. At least 53% of confirmed anti-HCV carriers had no detectable viral RNA and were considered to have cleared the virus and recovered from the infection. Confirmation was authenticated by the presence of antibodies specific to at least two viral antigens, mostly NS3 and E2. Reactivity to HCV core antigens was lower in Ghanaian than United Kingdom blood donors. The minority of chronically infected donors carried a viral load significantly lower than an unselected comparative group of United Kingdom blood donors (2.5 x 10(5) versus 2.9 x 10(6) IU/ml; P = 0.004). HCV genotype 2 was largely predominant (87%). Sequence clustering was similarly broad in the E1/E2 and NS5 regions. The phylogenetic diversity and the incapacity to distinguish subtypes within genotype 2 in our and others' West African strains suggested that West Africa may be the origin of HCV genotype 2. The genetic diversity extended to the identification of strains clearly separated from known subtypes of genotype 2 and genotype 1. One strain appears to be part of a new HCV genotype. HCV infection in Ghana is characterized by a high rate of recovery and the predominance of broadly divergent genotype 2 strains.
PMID: 12829831 [PubMed - indexed for MEDLINE]

68: JAMA. 2003 Jul 9;290(2):228-37.
Cost-effectiveness of treatment for chronic hepatitis C infection in an evolving patient population.
Salomon JA, Weinstein MC, Hammitt JK, Goldie SJ.
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CONTEXT: Approximately 2.7 million US individuals are chronically infected with the hepatitis C virus (HCV). As public health campaigns are pursued, a growing number of treatment candidates are likely to have minimal evidence of liver damage.
OBJECTIVE: To examine the clinical benefits and cost-effectiveness of newer treatments for chronic hepatitis C infection in a population of asymptomatic, HCV sero-positive but otherwise healthy individuals. DESIGN AND
SETTING: Cost-effectiveness analysis using a Markov model of the natural history of HCV infection and impact of treatment. We used an epidemiologic model to derive a range of natural history parameters that were empirically calibrated to provide a good fit to observed data on both prevalence of HCV seropositivity and time trends in outcomes related to HCV infection. PATIENTS: Cohorts of 40-year-old men and women with elevated levels of alanine aminotransferase, positive results on quantitative HCV RNA assays and serologic tests for antibody to HCV, and no histological evidence of fibrosis on liver biopsy. INTERVENTIONS:
Monotherapy with standard or pegylated interferon alfa-2b; combination therapy with standard or pegylated interferon plus ribavirin. MAIN OUTCOME MEASURES: Lifetime costs, life expectancy, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios. RESULTS: The probability of patients with chronic HCV developing cirrhosis over a 30-year period ranged from 13% to 46% for men and from 1% to 29% for women. The incremental cost-effectiveness of combination therapy with pegylated interferon for men ranged from 26 000 dollars to 64 000 dollars per QALY for genotype 1 and from 10 000 dollars to 28 000 dollars per QALY for other genotypes; and for women ranged from 32 000 dollars to 90 000 dollars for genotype 1 and from 12 000 dollars to 42 000 dollars for other genotypes. Because the benefits of treatment were realized largely in the form of improvements in health-related quality of life, rather than prolonged survivorship, cost-effectiveness ratios expressed as dollars per year of life
were substantially higher. Results were most sensitive to assumptions about the gains and decrements in health-related quality of life associated with treatment.
CONCLUSIONS: While newer treatment options for hepatitis C appear to be

reasonably cost-effective on average, these results vary widely across different patient subgroups and depend critically on quality-of-life assumptions. As the pool of persons eligible for treatment for HCV infection expands to the more general population, it will be imperative for patients and their physicians to consider these assumptions in making individual-level treatment decisions.
PMID: 12851278 [PubMed - indexed for MEDLINE]

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From the Centers for Disease Control and Prevention. Hepatitis C virus transmission from an antibody-negative organ and tissue donor--United States, 2000-2002.
[No authors listed]
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Effect on dyspnoea and hypoxaemia of inhaled N(G)-nitro-L-arginine methyl ester in hepatopulmonary syndrome.
Brussino L, Bucca C, Morello M, Scappaticci E, Mauro M, Rolla G.
Department of Medicina e Chirurgia, Ospedale Molinette, Torino, Italy.
Hepatopulmonary syndrome--a complication of chronic liver disease-is characterised by hypoxaemia, which results from widespread intrapulmonary vascular dilatations. Amplified production of pulmonary nitric oxide is thought to be important in development of this disorder in patients with liver cirrhosis. Here, we report a 64-year-old man with hepatopulmonary syndrome
associated with hepatitis-C-virus-related cirrhosis. We gave the patient nebulised N(G)-nitro-L-arginine methyl ester (L-NAME), an inhibitor of NO synthesis, which enhanced oxygenation (arterial oxygen pressure increased from 6.98 to 9.45 kPa). After L-NAME, the distance the patient could walk in 6 min rose by 92 m. Administration of L-NAME by aerosol might offer a new approach to treatment of hepatopulmonary syndrome.
PMID: 12853200 [PubMed - indexed for MEDLINE]

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Comment on:
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Clinical efficacy and toxiciy of gefitinib in patients with lung cancer.
Mitsui H, Nakajima J, Maruyama T, Hanajiri K, Omata M.
PMID: 12801776 [PubMed - indexed for MEDLINE]

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Low frequency of bcl-2 rearrangement in HCV-associated non-Hodgkin's lymphoma tissue.
Libra M, De Re V, De Vita S, Gasparotto D, Gloghini A, Rupolo M, Degan M, Marzotto A, Stivala F, Carbone A, Boiocchi M.
PMID: 12835744 [PubMed - indexed for MEDLINE]

73: MedGenMed. 2003 Mar 13;5(1):13.
A 50-year-old woman with massive splenomegaly and hepatitis C infection.
Hampel H.
Baylor College of Medicine, Houston, Texas, USA.
PMID: 12827074 [PubMed - indexed for MEDLINE]

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HCV/HIV--2003 retrovirus update.
Swan T.
PMID: 12866486 [PubMed - indexed for MEDLINE]

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Interferon alfacon-1: new preparation. Basically a me-too interferon alfa.
[No authors listed]
Interferon alfacon-1 differs from other interferon alfa preparations by only a few amino acids. In patients with chronic active hepatitis C, two comparative trials show that interferon alfacon-1 has the same activity and adverse effects as other interferons alfa. Interferon alfacon-1 is less easy to administer.
PMID: 12825573 [PubMed - indexed for MEDLINE]

76: Prim Care. 2003 Mar;30(1):81-107.
Hepatitis.
Marsano LS.
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Hepatitis is a common disorder with diverse etiology. Hepatitis can be classified as acute when duration is short and as chronic when it lasts more than 6 months. It can also be suspected to be chronic because of its cause. When evaluating a patient with hepatitis, investigation for viral etiologies is usually the first step, however it is important not to forget the other possibilities of drug- or chemical-related injury, as well as the multiple immune, metabolic and toxic causes of hepatitis. In this article, we have dedicated the larger part of our discussion to viral etiologies. There has been enormous progress over the past few years in the management of viral hepatitis, especially of viral hepatitis B and C. In this article, we discussed current therapeutic options in the management of these relatively common disorders and provided some recommendations in preventing transmission of these infections.
PMID: 12825251 [PubMed - indexed for MEDLINE]

77: Prof Nurse. 2003 Jun;18(10):553-4.
Blood-borne viral STIs.
Jones M.
Eastbourne Downs Primary Care Trust.
PMID: 12808852 [PubMed - indexed for MEDLINE]

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Injection practices in southern part of India.
Rajasekaran M, Sivagnanam G, Thirumalaikolundusubramainan P, Namasivayam K, Ravindranath C.
Department of Pharmacology, KAP Viswanatham Government Medical College, Trichy,
Tamilnadu, India. rajadoc@yahoo.com
The World Health Organization defines 'a safe injection' as one that does not harm the recipient, does not expose the provider to any avoidable risk, and does not result in any waste that is dangerous to the community. Irrational and unsafe injection practices are rife in developing countries. The objective of the present study was to assess the injection practices in the state of
Tamilnadu, India, using the Rapid assessment and response guide of the Safe Injection Global Network of the World Health Organization. Thirty-nine prescribers, 62 providers, and 175 members of the general public were interviewed. The areas were chosen out of convenience while at the same time adhering to the guidelines. The study was carried out between April and June 2001. The per capita injection rate

was 2.4 per year. The ratio of therapeutic to immunization injections was 6.5:1, and the proportion of injections given with a disposable syringe and needle was 35.4%. Knowledge about diseases transmitted by unsafe injections, for example involving human immunodeficiency virus and hepatitis B virus, was greater among all the study groups. The annual incidence of needlestick injuries among providers was 23.6, which is extremely high. It is concluded that there are deficiencies in practice such as an excessive, unwarranted usage of injections, a sizeable prevalence of unsafe injection practices, the short supply of injection equipment leading to a high incidence of needlestick injuries, a low proportion of hepatitis B virus immunization among providers, and a lack of adequate sharps containers and disposal facilities in this part of India. It is suggested that immediate and long-term remedial measures, such as the education of prescribers to reduce the number of injections to a bare minimum, an adequate supply of injection equipment, provider protection with immunization for hepatitis B virus, the provision of adequate sharps containers with safe disposal facilities and, not least, community education, be undertaken to avoid the future epidemic of transmissible diseases.
PMID: 12825472 [PubMed - indexed for MEDLINE]

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Hepatitis C seroprevalence among newly incarcerated inmates in the Texas correctional system.
Baillargeon J, Wu H, Kelley MJ, Grady J, Linthicum L, Dunn K.
Department of Pediatrics, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284-7802, USA. baillargeon@uthscsa.edu
The seroprevalence of hepatitis C (HCV) infection was examined among a sample of incoming inmates in the Texas Department of Criminal Justice (TDCJ) prison system. Rates were compared across demographic factors and three types of prison facilities: substance abuse felony punishment units (SAFPs), state jails and prisons. The study sample consisted of 3712 incoming inmates incarcerated for any duration, dating from 1 November 1998 to 31 May 1999. Among males, inmates entering SAFPs and state jails had comparable HCV infection rates (29.7 and 27.0%, respectively) to those entering prisons (27.3%). Among females, inmates
entering prisons had a higher rate of infection (48.6%) than those entering state jails (35.1%) or SAFPs (38.3%). For both genders, blacks exhibited a lower overall infection rate than whites and Hispanics, and HCV seroprevalence increased in a stepwise fashion with age. All subgroups of TDCJ inmates, including those held in alternative correctional facilities, exhibited HCV infection rates that were comparable with previous reports of inmate populations, but dramatically higher than general community samples. Given that most inmates held in alternative facilities will return to the general community in a short period of time, understanding the HCV infection rates in these subgroups holds particular public health relevance.
PMID: 12802904 [PubMed - indexed for MEDLINE]

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Detection of HCV-RNA in bronchoalveolar lavage from a woman with pulmonary fibrosis.
Brunetti G, Delmastro M, Nava S, Pignatti P, Bossi A, Gatti M, Furione M.
Respiratory Unit, Salvatore Maugeri Foundation, IRCCS, Pavia, Italy. gbrunetti@fsm.it
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Treatment for hepatitis C in patients infected with human immunodeficiency virus. [Article in English, Spanish]
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Servicio de Medicina del Aparato Digestivo. Hospital Universitario 12 de Octubre. Madrid. Spain.
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Seroprevalence of hepatitis B and C in maintenance dialysis in a public hospital in a developing country.
Otedo AE, Mc'Ligeyo SO, Okoth FA, Kayima JK. Department of Medicine, University of Nairobi, Kenya.
BACKGROUND: Patients with end-stage renal disease (ESRD) on maintenance dialysis are predisposed to hepatitis B virus (HBV) infection for a number of reasons. In a similar way, the prevalence of anti-hepatitis C virus (HCV) antibodies among patients on chronic haemodialysis and peritoneal dialysis is consistently higher than in healthy populations. There are few published data on these diseases in patients undergoing maintenance dialysis in sub-Saharan Africa. OBJECTIVE: To determine the seroprevalence of HBV and HCV in patients on maintenance dialysis. SETTING: Renal Unit, Kenyatta National Hospital, the largest public referral and teaching hospital in Kenya. DESIGN: Cross-sectional descriptive study. STUDY POPULATION: All 100 patients on maintenance dialysis during the 9-month study period were evaluated. METHOD: The following information was obtained from all the patients: socio-demographic data, date of diagnosis of ESRD and commencement of dialysis, and number of blood transfusions. Additionally, a history suggestive of hepatitis in spouses was looked for and physical examination for tattoos and other scars was carried out. Laboratory investigations included urea, electrolytes and serum creatinine, liver enzymes, hepatitis B surface antigen (HBsAg), immunoglobulin M anti-hepatitis B core antibody (IgM anti-HBc), hepatitis B e antigen (HBeAg) and anti-HCV antibodies. Student's t-test was used to assess the significance of the data collected. RESULTS: The results were expressed as mean (+/- SD). Fifty-seven males and 43 females were studied. Mean age was 44.3 +/- 14.6 years. Ten patients (10%) had elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (> 40 U/l for both).
HBsAg was found in 8 patients (8%), IgM anti-HBc in 2%, and HBeAg in none. Anti-HCV antibody was found in 5%. Six of the HBsAg-positive patients were on haemodialysis, the other 2 on continuous ambulatory peritoneal dialysis (CAPD). There was no coexistence of HBV and HCV markers. Longer duration of dialysis and the number of blood transfusions were associated with an increased seroprevalence of HBV and HCV. CONCLUSION: There is a low seroprevalence of HBV and HCV in our dialysis population. This should not lead to complaisance in screening for these potentially lethal complications.
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Detection of a healthy carrier of HCV with no evidence of antibodies for over four years.
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BACKGROUND: Posttransfusion HCV has been notably reduced over recent years as a
result of the systematic testing for antibodies to HCV in blood donors. However, the risk of transfusing blood-derived components from virus-carrying donors still remains. A diagnosis is reported here of HCV in a regular blood donor who had no antibodies during the entire time she was followed up. CASE REPORT: The pharmaceutical company responsible for fractioning the plasma detected a donor who was a carrier of HCV, confirmed by PCR, but whose tests to detect anti-HCV were systematically negative. The donor had given blood on five previous

occasions, from which 14 components were manufactured. Of the 11 components traced, six had been transfused, and in the two cases in which study of the anti-HCV was possible in the recipients, the result was positive. It was possible to check the blood samples from the donor from May 1997 to March 2002 (58 months). The tests to detect anti-HCV were all negative, while the PCR and core antigen tests were positive. CONCLUSION: The incorporation of RNA detection or HCV core antigen techniques in blood banks may reduce the residual risk of contracting posttransfusion HCV. Measures such as the correct traceability of the components, the existence of a specimen bank, or follow up of the recipients of blood-derived components would help to improve the quality of blood banking with percentage of survivability and case investigations.
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A new HCV core antigen assay based on disassociation of immune complexes: an alternative to molecular biology in the diagnosis of early HCV infection.
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BACKGROUND: An EIA based on immune complex disassociation of nucleocapsid proteins of HCV has been developed to detect and quantify HCV core antigen. STUDY DESIGN AND METHODS: To evaluate whether this new assay (trak-C, Ortho Clinical Diagnostics) could be an alternative to NAT during the window period, its sensitivity in this context was assessed, and its performance was compared with that of a first-generation HCV core antigen assay dedicated to the blood screening (HCV core antigen ELISA). Studied populations included nine HCV RNA-positive, HCV antibody-negative blood donors and 23 hemodialysis patients who underwent an HCV seroconversion. From these individuals, 81 samples (23 HCV RNA-negative and 58 HCV RNA-positive) sequentially collected during the phase before seroconversion were tested. RESULTS: The nine blood donor samples were positive for the presence of HCV core antigen by the trak-C, and 6 of 8 tested were positive for the presence of HCV core antigen by blood screening ELISA. In the hemodialysis cohort, the 23 HCV RNA-negative samples were negative with the two HCV core antigen assays. Among the 58 HCV RNA-positive samples, 46 of 57 (80.7%) tested were positive for the presence of HCV core antigen with the blood screening assay, and 57 of 58 (98.2%) were positive for the presence of HCV core antigen with the trak-C. The mean delays in detecting HCV infection between trak-C and the appearance of HCV antibodies, between HCV RNA testing and trak-C, and between trak-C and HCV core antigen ELISA were 58.2, 0.24, and 3.33 days, respectively. CONCLUSION: Trak-C was more sensitive than the blood screening assay and had similar performance to HCV RNA assay in the window period. Trak-C could constitute an alternative to NAT for the diagnosis of HCV infection during the window period, especially when molecular biology procedures cannot be implemented.
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